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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,978	11/26/2001	Yun-Peng Huang	33154-176173	5332

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VENABLE, BAETJER, HOWARD AND CIVILETTI, LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
LEWIS, PATRICK T	
ART UNIT	**PAPER NUMBER**
1623	7

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,978	HUANG ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-20 and 26-36* is/are pending in the application.

4a) Of the above claim(s) *28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-20,26,27 and 30-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *8*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Response dated July 28, 2003

1. In the Response filed July 28, 2003, claims 1, 3-4, 8-9, and 26; claims 11 and 21-25 were canceled; and claims 30-36 were added. Applicant presented arguments in the Response dated April 14, 2003. Applicant's response dated April 14, 2003 was deemed non-responsive because the marked up version of claims 21 and 27 do not reflect all the changes in the clean version relative to the previous version of said claims; however, applicant's arguments are deemed germane and thus have been fully considered. Claims 28-29, originally presented in the amendment dated April 14, 2003, have been withdrawn from consideration as applicant has failed to present said claims in the amendment dated July 28, 2003. The examiner suggests cancellation of said claims.

2. Claims 1-10, 12-20, and 26-36 are pending. An action on the merits of claims 1-10, 12-20, and 26-36 is contained herein below.

3. The objection to the specification has been rendered moot in view of applicant's amendment dated April 14, 2003.

4. The rejection of claims 1-27 under 35 U.S.C. 112, first paragraph, has been rendered moot in view of applicant's arguments dated April 14, 2003.

5. The rejection of claims 1-27 under 35 U.S.C. 112, second paragraph, has been rendered moot in view of applicant's amendments dated July 28, 2003.

6. The rejection of claims 1-10, 12-20, and 26-27 under 35 U.S.C § 103(a), is maintained for the reasons of record set forth in the Office Action dated January 14, 2003. The rejection of claims 11 and 21-25 has been rendered moot in view of applicant's amendment dated July 28, 2003.

Objections/Rejections of Record Set Forth in Office Action

Dated January 14, 2003

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1-10, 12-20, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gala et al. US 5,478,571 (Gala) in combination with Bai US 5,840,329 (Bai).

Applicant claims low-residual-solvent excipients comprising water-absorbing property, for instance a polysaccharide with a water-absorbing radical of formula $-RCOO^{-}A^{+}$. Applicant also claims methods for obtaining said low-residual-solvent excipients by mixing a solvent/water solution with said low-residual-solvent excipient, and removing the solvent via filtration and drying. Applicant claims various particular polysaccharides. In addition, applicant claims various solvent ratios and reaction conditions.

Gala teaches methods to remove residual solvent alcohols without adverse affects to the drug by adding a small amount of water (col. 2, lines 24-30). In particular, in col. 3, lines 45-57, Gala teaches that when the solvent content is from between about

20% to 1.5% w/w of the original amount, approximately 0.1% to about 5.0%, preferably about 2.1% water is added to the system which continues to run until nearly all the solvent(s) is removed. With subsequent drying, the amount of alcohol present in the drug carrier blend can be reduced to 0.1% [1000 ppm] or less. Gala teaches that the excipient blend of conventional carrier materials can be lactose, microcrystalline cellulose and cornstarch (col. 3, lines 28-33). In addition Gala teaches alcohols, such as ethanol, methanol or blend of methanol and ethanol, as suitable solvents.

Gala does not specifically disclose each of the particular polysaccharides claimed or excipients with water-absorbing properties. Further, Gala does not explicitly teach that the solvent can be acetone. Finally, Gala does not explicitly teach each of the various solvent ratios or reaction conditions.

Bai teaches that various polysaccharides, including acylated polysaccharides, are well known in the art to be suitable excipients. See col. 8, lines 12-39. In particular, Bai teaches that carboxymethylcellulose and sodium starch glycolate, polysaccharides with water-absorbing properties (i.e. containing $-CH_2$-O-R-COO^-A^+ moieties), are known as inert pharmaceutical excipients.

It would have been obvious to one of ordinary skill in the art to use the method of Gala to reduce the residual solvent content of any known drug/excipient system. Therefore, a skilled artisan would have been motivated and would have had a reasonable expectation of success to use any known conventional excipient, such as carboxymethylcellulose and sodium starch glycolate, which are acylated and thus have the disclosed water-absorbing properties, as taught by Bai, in the method provided by

Gala to obtain the low-residual-solvent excipient claimed in the present invention. Further, the choice of solvent and reaction conditions, i.e. temperature and agitation methods, are seen to be a choice of experimental design, are well known to one of ordinary skill and are well within the purview of the prior art.

Applicant's arguments filed April 14, 2003 have been fully considered but they are not persuasive. Applicant argues: 1) Gala does not teach that the excipient contains less than 3000 ppm of solvent and possess a water absorbing property which is characterized by the presence of the methoxy alkylcarboxyl group in the excipient and 2) Bai teaches away from the instant invention. The examiner strongly disagrees with applicant's characterization of the art of record.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

As set forth supra, Gala does indeed teach that the excipient compositions contains less than 3000 ppm. Applicant's attention is directed to col. 3, lines 53-55, wherein Gala explicitly teaches that the amount of solvent in the composition is reduced to 1000 ppm or less. The examiner further disagrees with applicant's characterization of Bai. Contrary to applicant's assertion carboxymethylcellulose and sodium starch glycolate do indeed contain $-CH_2$-O-R-COO^-A^+ moieties and thus contain the "water absorbing property" as claimed by applicant.

All of the limitations or absolute predictability is not required to establish *prima facie* obviousness. The art of record is good for what it shows. Applicant's arguments are not convincing in view of that which the prior art teaches as a whole. In the absence of some proof of a secondary nature to obviate the rejection as set forth in the Office Action dated January 14, 2003, or of some specific limitations which would tip the scale of patentability in the favor of the instantly claimed invention, the rejection is maintained.

Claim Objections

9. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 28-34 been renumbered 30-36.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "water absorbing property" renders the claims in which it appears indefinite. In the absence of distinct modifications to the excipient claimed or distinct

language to describe the structural modifications or the chemical names of the excipients of this invention, the identity of said property would be difficult to describe and the metes and bounds of said modified compounds applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 30-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gala et al. US 5,478,571 (Gala) in combination with Bai US 5,840,329 (Bai) as applied to claims 1-10, 12-20, and 26-27 above, and further in view of Bahia et al. US 6,075,177 (Bahia).

Claims 30-34 depend from claim 13 and are drawn to a method of producing a low-residual-solvent excipient comprising mixing a solvent/water solution with said low-residual-solvent excipient, and removing the solvent via filtration and drying. Claims 30-34 further comprise the step of attaching a water-absorbing radical to said low-residual solvent-excipient before said low-residual-solvent excipient mixes with said solvent-water solution. Claims 35-36 are drawn to a low-residual-solvent excipient which has residual solvent of less than 3000 ppm and possesses water absorbing property; wherein said low-residual-solvent excipient is a gelatinized starch.

Neither gala nor Bai explicitly teach the synthesis of low-residual-solvent excipient (i.e. synthesis of carboxymethylcellulose). However, their synthesis is well-known in the art as shown by Bahia.

Bahia teaches that carboxymethylcellulose is prepared by reacting cellulose with a strong alkali and with monochloroacetic acid or a salt thereof (column 3, lines 11-13; column 4, lines 5-16). The monochloroacetic reagent is preferably used in salt form, usually corresponding to the alkali used, for example sodium monochloroacetate with sodium hydroxide.

It would have been obvious to one of ordinary skill in the art to use the method of Gala to reduce the residual solvent content of any known drug/excipient system. Therefore, a skilled artisan would have been motivated and would have had a reasonable expectation of success to use any known conventional excipient, such as carboxymethylcellulose and sodium starch glycolate, which are acylated and thus have the disclosed water-absorbing properties, as taught by Bai, in the method provided by Gala to obtain the low-residual-solvent excipient claimed in the present invention. Further, the choice of solvent and reaction conditions, i.e. temperature and agitation methods, are seen to be a choice of experimental design, are well known to one of ordinary skill and are well within the purview of the prior art.

Conclusion

16. Claims 1-10, 12-20, and 26-36 are pending. Claims 28-29 are withdrawn from consideration. Claims 1-10, 12-20, 26-27 and 30-36 are rejected. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

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April 2, 2004